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(54) Storage of materials.

(57) A material or mixture of materials which is not itself storage stable is rendered storage stable by incorporation into a water-soluble or swellable glassy or rubbery composition which can then be stored at ambient temperature. Recovery is by adding aqueous solution to the composition.

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STORAGE OF MATERIALS

This invention relates to the stabilisation and storage of materials. The principal envisaged field of application is materials employed in the biochemical field and some pharmaceuticals.

A few biologically active materials (e.g. some proteins) are sufficiently stable that they can be isolated, purified and then stored in solution at room temperature. For most materials however this is not possible and some more elaborate form of stabilisation/storage procedure must be used.

A "repertoire" of techniques is known. Not all of them are useful for all materials that give rise to a storage problem. Known storage/stabilisation techniques which are applied to materials after isolation into an aqueous suspension or solution are:-

(i) Addition of high concentration of chemical "stabilizer" to the aqueous solution or suspension. Typically 3M ammonium sulphate is used. However, such additives can alter the measured activity of enzymes and can give ambiguous or misleading results if the enzyme is used in a test procedure. (R. H. M. Hatley and F. Franks, Variation in apparent enzyme activity in two-enzyme assay systems: Phosphoenol-pyruvate carboxylase and malate dehydrogenase, Biotechnol. Appl. Biochem. 11 367-370 (1989)). In the manufacture of diagnostic kits based on multi-enzyme assays, such additives often need to be removed before the final formulation. Such removal, by dialysis, often reduces the activity of an enzyme.

(ii) Freeze/thaw methods in which the preparation, usually mixed with an additive (referred to as a cryoprotectant) is frozen and stored, usually below -50°C, sometimes in liquid nitrogen. Not all proteins will survive a freeze/thaw cycle.

(iii) Cold storage, with a cryoprotectant additive present in sufficient concentration (e.g. glycerol) to depress the freezing point to below the storage temperature and so avoid freezing. For example in the case of restriction endonucleases, the enzymes need to be protected against freezing by the addition of high concentrations of glycerol and maintained at -20°C. Use of an additive in high concentration may also reduce the specificity of restriction enzymes and give rise to so-called "star-activity". (B. Polisky et al. PNAS USA, 72, 3310 (1975)).

(iv) The commonest method for the stabilisation of isolated protein preparations is freeze-drying, but this process can only be applied to freeze-stable products. The aqueous isolate of the active material in a suitable pH buffer and in the presence of a cryoprotectant is first frozen, typically to -40° to -50°C; the ice is then removed by sublimation under vacuum and at low subzero temperatures, following which the residual moisture which may amount up to 50% of the "dried" preparation is removed by desorption during which the temperature gradually rises. The complete freeze-drying cycle may take several days and is costly in capital and energy. Freeze-drying also suffers from technical disadvantages because of its irreproducibility. Suppliers of freeze-dried protein products generally specify storage at -20°C rather than ambient temperature. Exposure to ambient temperatures for periods of days to weeks can result in significant activity losses.

(v) Undercooling, as described in European Patent 0 138 030 and by Hatley et al. (Process Biochem. 22 169 (1987)) allows for the long-term (years) stabilisation of proteins without the need for additives. However, while this process extended the previous repertoire of possibilities, the undercooled preparations need to be shipped at temperatures not exceeding +5°C and must be stored, preferably at -20°C. They also have to be recovered from a water-in-oil dispersion prior to their final use.

It will thus be apparent that a stabilisation/storage process which enabled storage at ambient temperature would be very desirable, since it would avoid the need for low temperature storage entailed by existing processes. Hitherto, however, storage at ambient temperature has been impossible for many materials.

There would also be advantage in adding to the existing "repertoire" of processes for stabilisation and storage, because some of the existing processes are limited in their applications or entail accepting disadvantages such as a need to mix with a stabilising agent which is difficult to remove later.

There would furthermore be advantage in providing a more cost effective process than the current freeze-drying process.

We have found, surprisingly, that materials which are not stable when isolated and held in solution at room temperature can nevertheless be successfully incorporated into a glass formed from a water-soluble or water-swellable substance, and can later be recovered. While in the glass the material is immobilised and stable.

In a first aspect this invention provides a storable composition comprising at least one material to be stored, preferably selected from the group consisting of proteins, peptides, nucleosides, nucleotides and enzyme cofactors, dissolved in a water-soluble or water-swellable substance which is in an amorphous, glassy or (much less preferably) rubbery state.